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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/642,289	08/18/2003	Stuart Maxwell Pitson	PITSON1A	2015

1444 7590 07/01/2005

BROWDY AND NEIMARK, P.L.L.C.
624 NINTH STREET, NW
SUITE 300
WASHINGTON, DC 20001-5303

EXAMINER	
MONSHIPOURI, MARYAM	

ART UNIT	PAPER NUMBER
1653	

DATE MAILED: 07/01/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/642,289	PITSON ET AL.	
	Examiner	Art Unit	
	Maryam Monshipouri	1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) 1-12 is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) 1-12 is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☒ Certified copies of the priority documents have been received in Application No. 09/959,897.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date 5/15&8/18/03.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☒ Other: See attachment

Applicant's response to restriction requirement filed on 6/2/2005 is acknowledged. Applicant elected Group I invention, directed to sphingosine kinase, derivatives, mimetic etc, thereof and pharmaceutical compositions comprising all said products, without traverse.

DETAILED ACTION

Claims 1-12 are under examination on the merits.

Priority

It is noted that applicant refers to the priority data in first page of the specification. However. Said reference is not up to date. Applicant is requested too update all priority information underneath the title in response to this office action.

In addition it is acknowledged that applicant claims foreign priority to two Australian patents, certified copies of which have been submitted in the patent case of this application. It is requested that copies of said documents to be resubmitted in the instant case for clarity of record.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-4, 6-10, and 12 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The terms "analogue", "derivative", "chemical equivalent" and "mimetic" in claims 1-4 and 6 (as well as their dependent claims 7-10 and 12) are unclear. Applicant has not defined said terms in the

specification. For example, it is indefinite as to whether analogues, and derivatives refer to structural homologs of sphingosine kinase or its functional homologs etc. Appropriate clarification is required.

Claims 3, 4 and 9-10 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. It is indefinite as to what a derivative, or mimetic of a derivative, analogue, chemical equivalent or mimetic of SEQ ID NO:2 or its "substantial" homolog (see claims 3-4 and their dependent claims 9-10) is.

Claims 6 and 12 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. It is unclear as to how the phrase "for use in modulating cellular functional activity" is contributing to claim 6 and its dependent claim 12 . If, in fact, said phrase does contribute to the product claimed it is unclear as to which specific cellular functional activity is claimed. Appropriate clarification us required.

Claims 4 and 10 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The term "low stringency" in claim 4 and its dependent claim 10 is unclear. Applicant has not defined said term specifically in the specification. In page 21, applicant refers to low stringency conditions as including 0%-15% v/v formamaide and from at least 1M to at least 2M salt for hybridization etc. Said conditions do not clarify the exact salt and temperature conditions used in claim 4 such that the skilled artisan could utilize said conditions to prepare the products claimed.

Claims 5 and 11 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The term "substantially" in claim 5 is unclear. Applicant has not defined said term in the specification. If said term has the same structural limitations as in claim 3 applicant is advised to recite said limitation into claim 5 after reviewing the 112 first rejection drafted below. Appropriate clarification is required.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-4, 6-12 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Claims 1-2 and 6 are directed to products (such as a **genus** of sphingosine kinase analogues, chemical equivalents, derivatives and mimetis) which are merely claimed by their function. While claims 3-5 recite some structure which is inadequate to define the **genus** of sphingosine kinases as broadly claimed.

With respect to claims 1-2 and 6 the court of Appeals for the Federal Circuit has recently held that such a general definition does not meet the requirements of 35 U.S.C. 112, first paragraph. " A written description of an invention involving chemical

genus, like a description of a chemical species, requires a precise definition, such as be structure, formula {or} chemical name, of the claimed subject matter sufficient to distinguish it from other materials." *University of California v. Eli Lilly and Co.,* 1997 U.S. App. LEXIS 18221, at *23, quoting *Fiers v. Revel,* 25 USPQ2d 1601, 1606 (Fed. Cir. 1993). The court held that " in claims involving chemical materials, generic formulae usually indicate with specificity what generic claims encompass. One skilled in the art can distinguish such a formula fro others and can identify many of the species that the claims encompass. accordingly, such a formula is normally an adequate description of the claimed genus. In claims to genetic material, however, a generic statement such as "vertebrate insulin cDNA" or "mammalian insulin cDNA,' without more, is not an adequate written description of the genus because it does not distinguish it from others. One skilled in the art therefore cannot, as one can do with a fully described genus visualize the identity of the members of the genus". Here, applicant is claiming a **genus** of kinases merely by function. Said claim does not teach any structural means of distinguishing claimed products from say other mammalian members of the genus rendering the claims 1-2 and 6 (and their dependent claims 7-8 and 12) subject to written description rejection.

With respect to claims 3 and 9, applicant is reminded that a protein comprising a sequence having at least 45% similarity to 10 contiguous amino acids of SEQ ID NO:2, needs merely to comprise 5 (10X0.45=4.5, which is approximately 5) contiguous amino acids of SEQ ID NO:2. Such a broad genus comprises many polypeptides that have nothing in common either structurally or functionally with the products claimed instantly.

This is because kinases require at least 250-300 amino acids corresponding to their catalytic site in order to retain any activity and 5 amino acids is totally incapable or retaining any function whatsoever.

Similarly the products recited in claim 4 are merely encoded by DNA sequences that hybridize to SEQ ID NO:1, under low stringency conditions. Said conditions are not defined specifically in the specification (see page 21). Thus, many DNA sequences capable of encoding products unrelated to kinase of this invention can hybridize to SEQ ID NO:1, under said "low stringency conditions", rendering claim 4 (and its dependent claim 10) subject to written description rejection.

Likewise the genus of sphingosine kinase, equivalents, derivatives, mimetics etc. (in claim 5 and its dependent claim 11) are inadequately described in terms of structure (see the 112 second rejection above). It is unclear as how to recognize the members of the claimed genus from others.

Therefore the genera of polypeptides and homologs thereof in claims 3-5 (and their dependent claims 9-11),defined merely by a **single species** (namely SEQ ID NO:2) and are subject to lack of written description rejection for lacking sufficient structural information, lacking function or lacking both.

Applicant is referred to the revised interim guidelines concerning compliance with the written description requirement of U.S.C. 112, first paragraph, published in the Official Gazette and also available at www.uspto.gov.

Claims 3-5 and 7-12 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for SEQ ID NO:2 and compositions comprising

said products and a pharmaceutically acceptable carrier, does not reasonably provide enablement for proteins comprising homologs of SEQ ID NO:2, as recited in claims 3-5 with no function or pharmaceutical compositions comprising said products.

The criteria for undue experimentation, summarized in *re Wands*, 8, USPQ2n 1400 (Fed. Cir. 1988) are: 1) the quantity of experimentation necessary, 2) the amount of direction or guidance presented, 3) the presence and absence of working examples, 4) the nature of the invention, 5) the state of prior art, 6) the relative skill of those in the art, 7) the predictability or unpredictability of the art, and 8) the breadth of the claims.

The specifications fails to teach which residues beyond 5 contiguous amino acids of SEQ ID NO:2 (see claim 3) must be present such that claimed homologs, derivatives, mimetics thereof retain sphingosine kinase function. The specification is also silent about which residues in either proteins "substantially" as set forth in SEQ ID NO:2 (see claim 5) or proteins that are encoded by a DNA sequence that hybridizes to SEQ ID NO:1 under low stringency conditions (see claim 4) must be retained such that said homologs retain kinase activity. No examples of such residues are provided either. Current state of prior art indicates that 5 contiguous amino acids is totally incapable of rendering function to any polypeptides and polypeptides "substantially" as set forth in a full-length polypeptide or encoded by a DNA sequence that hybridizes to a full-length polypeptide encoding sequence under low stringency conditions, do not necessarily retain the function of said full-length polypeptide.

Therefore due to lack of sufficient guidance, and examples provided in the specification and due to unpredictability of prior art as to which polypeptides that merely

comprise 5 contiguous amino acids of a full-length polypeptide or that are "substantial" homologs of said polypeptide or encoded by a DNA sequence that hybridizes to that encoding a full-length polypeptide under low stringency conditions are capable of encoding a product with function associated with said full-length polypeptide one of skill in the art has to go through the burden of undue experimentation in order to screen for those products that have sphingosine kinase activity and as such the claims go beyond the scope of the disclosure.

Since claims 3-5 are not enabled their dependent claims 9-11 are not enabled either.

With respect to "pharmaceutical composition" language used in claims 7-12 It is well known in the art that for any agent to be used as a pharmaceutical composition, an effective dose of that specific agent and the disease/disorder/ condition against which it is used is required. Further when new agents are to be used in a pharmaceutical composition, there is also a need for the demonstration that the agent would be effective in the said dosage against a specific disease/disorder/condition in an art accepted animal model experiment/s. Without such information one skilled in the art would be unable to make and use the claimed invention without undue experimentation. However, in this case the specification fails to provide such details.

The specification does not enable the use of a pharmaceutical composition of human sphingosine kinase because the specification does **not** establish/provide :(A)the effective amount of kinase needed for use in a pharmaceutical composition; (B) guidance as to what disease/disorder/condition the pharmaceutical composition is

effective against; and (C)demonstrate the desired effect of use in an art recognized animal model experiment.

Thus, applicants have not provided sufficient guidance to enable one of ordinary skill in the art to make and use the claimed invention drawn to a pharmaceutical composition of human sphingosine kinase. Without sufficient guidance, determination of pharmaceutical compositions having the desired characteristics is unpredictable and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue. See In re Wands 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988) recited above.

Applicant may overcome this rejection by deleting the term "pharmaceutical" in claims 7-12.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

Claims 1, 3-7, 9-12 are rejected under 35 U.S.C. 102(a) as being anticipated by Kohama et al. (J.B.C., 273(37), 23722-23728, 11/1998, cited in the IDS). Kohama teaches a murine sphingosine kinase that has 80.7% identity to SEQ ID NO:2 of this invention, having a sequence substantially as set forth in SEQ ID NO:2, which may be used for modulating "cellular functional activity", anticipating claims 1 and 5-6.

Kohama's sequence does comprise an amino acid sequence having at least 45% similarity to at least 10 contiguous amino acids of SEQ ID NO:2 (see the attached sequence alignment) and is encoded by a DNA sequence that hybridizes to SEQ ID NO:1, under 'low stringency conditions" , anticipating claims 3-4. In page 23723 Kohama teaches about methods of preparing buffers containing sphingoine kinase, wherein cells containing said kinase were lysed in Tris buffer (pH 7.4) and cell lysates were centrifuges in order to separate cytosol from membrane fractions. Said fractions can be considered to a pharmaceutical compositions comprising sphingosin kinases of this invention anticipating claims 7, 9-12.

> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 1-12 are rejected under 35 U.S.C. 102(e) as being Young et al. (U.S. Patent No. 6,525,174, issued 2/25/2003). Young teaches a human protein (see SEQ ID NO:328) that has 79.6% identity to SEQ ID NO:2 of this invention and inherently has sphingosin kinase activity (see the attached sequence alignment) prior to this application. Said sequence can be considered to be a derivative of SEQ ID NO:2, substantially as set forth as SEQ ID NO:2, to comprise at least 5 contiguous amino acids of SEQ ID NO:2, to be encoded by a DNA sequence that can hybridize to SEQ ID NOI:1 under low stringency conditions, and to be used for modulating cellular functional activity, anticipating claims 1-6. In column 305 Young teaches about pharmaceutical compositions comprising its polypeptides, anticipating claims 7-12 of this invention.

No claims are allowed.

Note:

SEQ ID NO:2 is allowed. This is because said sequence is free of prior art. Further the prior art does not teach or suggest preparing such specifically claimed amino acid sequence. Hence said sequence is also non-obvious.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Maryam Monshipouri whose telephone number is (571) 272-0932. The examiner can normally be reached on 7:00 a.m to 4:30 p.m. except for alternate Mondays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnanthapu Achutamurthy can be reached on (571) 272-0928. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

M. Monshipouri

Maryam Monshipouri Ph.D.

Primary Examiner

***

Attachment please send to applicant

TITLE OF INVENTION: Sphingosin Kinase, Cloning, Expression and Methods of Use
FILE REFERENCE: 07320001aa (2033957-0001)
CURRENT APPLICATION NUMBER: US/09/796,487
CURRENT FILING DATE: 2001-03-02
PRIOR APPLICATION NUMBER: US 60/186,532
PRIOR FILING DATE: 2000-03-03
PRIOR APPLICATION NUMBER: US 09/530,868
PRIOR FILING DATE: 2000-05-05
NUMBER OF SEQ ID NOS: 17
SOFTWARE: PatentIn version 3.1
SEQ ID NO 4
LENGTH: 381
TYPE: PRT
ORGANISM: Mus musculus
FEATURE:
NAME/KEY: MISC_FEATURE
LOCATION: (1)..(381)
OTHER INFORMATION: SEQ ID NO 4 is the peptide sequence of mSPHK1a in Figure 3, corre
OTHER INFORMATION: sponding to amino acid residue 124 to 504 of SPHK1a of GenBank se
OTHER INFORMATION: quence Accession Number AF068748. SEQ ID NO 4 is equivalent to SE
OTHER INFORMATION: Q ID NO 1 that is the amino acid sequence of SPHK1a in Figure 1.
PUBLICATION INFORMATION:
AUTHORS: Kohama et al.,
TITLE: Molecular cloning and functional characterization of murine sphingosine
TITLE: kinase
JOURNAL: Journal of Biological Chemistry
VOLUME: 273
ISSUE: 37
PAGES: 23722-23728
DATE: 1998
DATABASE ACCESSION NUMBER: AAC61697
DATABASE ENTRY DATE: 1998-09-26
RELEVANT RESIDUES: (124)..(504)
PUBLICATION INFORMATION:
DATABASE ACCESSION NUMBER: AAC61697
DATABASE ENTRY DATE: 1998-09-26
RELEVANT RESIDUES: (124)..(504)
US-09-796-487-4

Query Match 80.5%; Score 1624.5; DB 4; Length 381;
Best Local Similarity 81.2%; Pred. No. 1.1e-174;
Matches 306; Conservative 34; Mismatches 36; Indels 1; Gaps 1;

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Qy          7 PRGVLPRPCRVLVLLNPRGGKGKALQLFRSHVQPLLAEAEISFTLMLTERRNHARELVRS 66
              |||:|||||||||||||:|||||||||:| ||| | |||||:| |:|||||:|||||||| :
Db          6 PRGLLPRPCRVLVLLNPQGGKGKALQLFQSRVQPFLEEAEITFKLILTERKNHARELVCA 65

Qy         67 EELGRWDALVVMSGDGLMHEVVNGLMERPDWETAIQKPLCSLPAGSGNALAASLNHYAGY 126
              |||| |||| |||||||||||||||||||||||||||||||||| |||||||||:|||||||
Db         66 EELGHWDALAVMSGDGLMHEVVNGLMERPDWETAIQKPLCSLPGGSGNALAASVNHYAGY 125

Qy        127 EQVTNEDLLTNCTLLLCRRLLSPMNLLSLHTASGLRLFSVLSLAWGFIADVDLESEKYRR 186
              |||||||| |||||||| |||||||||||||||:|||||:|||:||||||||||||||||
Db        126 EQVTNEDLLINCTLLLCRRRLSPMNLLSLHTASGLRLYSVLSLSWGFVADVDLESEKYRR 185

Qy        187 LGEMRFTLGTPLRLAALRTYRGRLAYLPVGRVGSKTPASPVVVQQGPVDAHLVPLEEPVP 246
              |||:|||:||| |||:|| |:|:|||||| | || |||  :||:|||| ||||||||||
Db        186 LGEIRFTVGTFFRLASLRIYQGQLAYLPVGTVASKRPAS-TLVQKGPVDTHLVPLEEPVP 244

Qy        247 SHWTVVPDEDFVLVLALLHSHLGSEMFAAPMGRCAAGVMHLFYVRAGVSRAMLLRLFLAM 306
              |||||||::||:||| |||:|| |:|||||||| |||||||||||||||| ||||||||
Db        245 SHWTVVPEQDFLLVLVLLHTHLSSELFAAPMGRCEAGVMHLFYVRAGVSRAALLRLFLAM 304

Qy        307 EKGRHMEYECPYLVYVPVVAFRLEPKDGKGMFAVDGELMVSEAVQGQVHPNYFWMVSGCV 366
              :||:||| :|||||:||||||||||:  :|:|:|||||||| |||||||||| ||| |
Db        305 QKGKHMELDCPYLVHVPVVAFRLEPRSQRGVFSVDGELMVCEAVQGQVHPNYLWMVCGSR 364

Qy        367 EPPPSWKPQQMPPPEEP 383
              : |    :: ||||||
Db        365 DAPSGRDSRRGPPPEEP 381
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RESULT 12

US-09-796-487-5
; Sequence 5, Application US/09796487
; Patent No. 6830916
; GENERAL INFORMATION:
; APPLICANT: Spiegel, Sarah
; TITLE OF INVENTION: Sphingosin Kinase, Cloning, Expression and Methods of Use
; FILE REFERENCE: 07320001aa (2033957-0001)
; CURRENT APPLICATION NUMBER: US/09/796,487
; CURRENT FILING DATE: 2001-03-02
; PRIOR APPLICATION NUMBER: US 60/186,532
; PRIOR FILING DATE: 2000-03-03
; PRIOR APPLICATION NUMBER: US 09/530,868
; PRIOR FILING DATE: 2000-05-05
; NUMBER OF SEQ ID NOS: 17
; SOFTWARE: PatentIn version 3.1
; SEQ ID NO 5
; LENGTH: 373
; TYPE: PRT
; ORGANISM: Mus musculus
; FEATURE:
; NAME/KEY: MISC_FEATURE
; LOCATION: (1)..(373)
; OTHER INFORMATION: SEQ ID NO 5 is the peptide sequence of Mouse SPHK1a in Fig. 2, co
; OTHER INFORMATION: rresponding to amino acid residue 131 to 504 of SPHK1a of GenBank
; OTHER INFORMATION: sequence Accession Number AAC61697.
; PUBLICATION INFORMATION:
; DATABASE ACCESSION NUMBER: AAC61697
; DATABASE ENTRY DATE: 1998-09-26
; RELEVANT RESIDUES: (132)..(504)
US-09-796-487-5

Query Match 79.6%; Score 1606.5; DB 4; Length 373;
Best Local Similarity 81.0%; Pred. No. 1.2e-172;
Matches 303; Conservative 34; Mismatches 36; Indels 1; Gaps 1;

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Qy         10 VLPRPCRVLVLLNPRGGKGKALQLFRSHVQPLLAEAEISFTLMLTERRNHARELVRSEEL 69
              :|||||||||||||:|||||||||:| ||| | |||||:| |:|||||:|||||||| :|||
Db          1 LLPRPCRVLVLLNPQGGKGKALQLFQSRVQPFLEEAEITFKLILTERKNHARELVCAEEL 60

Qy         70 GRWDALVVMSGDGLMHEVVNGLMERPDWETAIQKPLCSLPAGSGNALAASLNHYAGYEQV 129
              | |||| |||||||||||||||||||||||||||||||||| |||||||||:|||||||||
Db         61 GHWDALAVMSGDGLMHEVVNGLMERPDWETAIQKPLCSLPGGSGNALAASVNHYAGYEQV 120

Qy        130 TNEDLLTNCTLLLCRRLLSPMNLLSLHTASGLRLFSVLSLAWGFIADVDLESEKYRRLGE 189
              |||||| |||||||| |||||||||||||||:|||||:|||:|||||||||||||||||
Db        121 TNEDLLINCTLLLCRRRLSPMNLLSLHTASGLRLYSVLSLSWGPVADVDLESEKYRRLGE 180

Qy        190 MRFTLGTPLRLAALRTYRGRLAYLPVGRVGSKTPASPVVVQQGPVDAHLVPLEEPVPSHW 249
              :|||:||| |||:|| |:|:|||||| | || |||  :||:|||| ||||||||||||
Db        181 IRFTVGTFFRLASLRIYQGQLAYLPVGTVASKRPAS-TLVQKGPVDTHLVPLEEPVPSHW 239

Qy        250 TVVPDEDFVLVLALLHSHLGSEMFAAPMGRCAAGVMHLFYVRAGVSRAMLLRLFLAMEKG 309
              ||||::||:||| |||:|| |:|||||||| |||||||||||||||| ||||||||:||
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Qy        310 RHMEYECPYLVYVPVVAFRLEPKDGKGMFAVDGELMVSEAVQGQVHPNYFWMVSGCVEPP 369
              :||| :|||||:||||||||||:  :|:|:|||||||| |||||||||| ||| | : |
Db        300 KHMELDCPYLVHVPVVAFRLEPRSQRGVFSVDGELMVCEAVQGQVHPNYLWMVCGSRDAP 359

Qy        370 PSWKPQQMPPPEEP 383
              :: ||||||
Db        360 SGRDSRRGPPPEEP 373
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RESULT 13
US-09-205-258-328
; Sequence 328, Application US/09205258
; Patent No. 6525174
; GENERAL INFORMATION:
; APPLICANT: Young et al.
; TITLE OF INVENTION: 207 Human Secreted Proteins
; FILE REFERENCE: PZ007P1
; CURRENT APPLICATION NUMBER: US/09/205,258

Attachment, please send to applicant

```
Db        66 EELGHWDALAVMSGDGLMHEVVNGLMERPDWETAIQKPLCSLPGGSGNALAASVNHYAGY 125

Qy       127 EQVTNEDLLTNCTLLLCRRLLSPMNLLSLHTASGLRLFSVLSLAWGFIADVDLESEKYRR 186

Db       126 EQVTNEDLLINCTLLLCRRRLSPMNLLSLHTASGLRLYSVLSLSWGFVADVDLESEKYRR 185

Qy       187 LGEMRFTLGTFLRLAALRTYRGRLAYLPVGRVGSKTPASPVVVQQGPVDAHLVPLEEPVP 246

Db       186 LGEIRFTVGTFFRLASLRIYQGQLAYLPVGTVASKRPAS-TLVQKGPVDTHLVPLEEPVP 244

Qy       247 SHWTVVPDEDFVLVLALLHSHLGSEMFAAPMGRCAAGVMHLFYVRAGVSRAMLLRLFLAM 306

Db       245 SHWTVVPEQDFVLVLVLLHTHLSSELFAAPMGRCEAGVMHLFYVRAGVSRAALLRLFLAM 304

Qy       307 EKGRHMEYECPYLVYVPVVAFRLEPKDGKGMFAVDGELMVSEAVQGQVHPNYFWMVSGCV 366

Db       305 QKGKHMELDCPYLVHVPVVAFRLEPRSQRGVFSVDGELMVCEAVQGQVHPNYLWMVCGSR 364

Qy       367 EPPPSWKPQQMPPPEEP 383

Db       365 DAPSGRDSRRGPPPEEP 381
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RESULT 8

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O88886
ID   O88886      PRELIMINARY;      PRT;   388 AA.
AC   O88886;
DT   01-NOV-1998 (TrEMBLrel. 08, Created)
DT   01-NOV-1998 (TrEMBLrel. 08, Last sequence update)
DT   01-MAR-2004 (TrEMBLrel. 26, Last annotation update)
DE   Sphingosine kinase.
GN   Name=Sphk1; Synonyms=SPHK1b;
OS   Mus musculus (Mouse).
OC   Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;
OC   Mammalia; Eutheria; Rodentia; Sciurognathi; Muridae; Murinae; Mus.
OX   NCBI_TaxID=10090;
RN   [1]
RP   SEQUENCE FROM N.A.
RX   MEDLINE=98395082; PubMed=9726979; DOI=10.1074/jbc.273.37.23722;
RA   Kohama T., Olivera A., Edsall L., Nagiec M.M., Dickson R., Spiegel S.;
RT   "Molecular cloning and functional characterization of murine
RT   sphingosine kinase.";
RL   J. Biol. Chem. 273:23722-23728(1998).
DR   EMBL; AF068749; AAC61698.1; -.
DR   MGD; MGI:1316649; Sphk1.
DR   GO; GO:0004143; F:diacylglycerol kinase activity; IEA.
DR   GO; GO:0007205; P:protein kinase C activation; IEA.
DR   InterPro; IPR001206; DAGKc.
DR   Pfam; PF00781; DAGK_cat; 1.
DR   ProDom; PD005043; DAGKc; 1.
DR   SMART; SM00046; DAGKc; 1.
KW   Kinase.
SQ   SEQUENCE   388 AA;  43254 MW;  01EB032322542CAD CRC64;
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Query Match 80.7%; Score 1627.5; DB 2; Length 388;
Best Local Similarity 81.4%; Pred. No. 5e-130;
Matches 307; Conservative 33; Mismatches 36; Indels 1; Gaps 1;

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Qy         7 PRGVLPRPCRVLVLLNPRGGKGKALQLFRSHVQPLLAEAEISFTLMLTERRNHARELVRS 66

Db        13 PRGLLPRPCRVLVLLNPQGGKGKALQLFQSRVQPFLEEAEITFKLILTERKNHARELVCA 72

Qy        67 EELGRWDALVVMSGDGLMHEVVNGLMERPDWETAIQKPLCSLPAGSGNALAASLNHYAGY 126

Db        73 EELGHWDALAVMSGDGLMHEVVNGLMERPDWETAIQKPLCSLPGGSGNALAASVNHYAGY 132

Qy       127 EQVTNEDLLTNCTLLLCRRLLSPMNLLSLHTASGLRLFSVLSLAWGFIADVDLESEKYRR 186

Db       133 EQVTNEDLLINCTLLLCRRRLSPMNLLSLHTASGLRLYSVLSLSWGFVADVDLESEKYRR 192

Qy       187 LGEMRFTLGTFLRLAALRTYRGRLAYLPVGRVGSKTPASPVVVQQGPVDAHLVPLEEPVP 246

Db       193 LGEIRFTVGTFFRLASLRIYQGQLAYLPVGTVASKRPAS-TLVQKGPVDTHLVPLEEPVP 251

Qy       247 SHWTVVPDEDFVLVLALLHSHLGSEMFAAPMGRCAAGVMHLFYVRAGVSRAMLLRLFLAM 306

Db       252 SHWTVVPEQDFVLVLVLLHTHLSSELFAAPMGRCEAGVMHLFYVRAGVSRAALLRLFLAM 311

Qy       307 EKGRHMEYECPYLVYVPVVAFRLEPKDGKGMFAVDGELMVSEAVQGQVHPNYFWMVSGCV 366

Db       312 QKGKHMELDCPYLVHVPVVAFRLEPRSQRGVFSVDGELMVCEAVQGQVHPNYLWMVCGSR 371

Qy       367 EPPPSWKPQQMPPPEEP 383

Db       372 DAPSGRDSRRGPPPEEP 388
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RESULT 9

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O88885
ID   O88885      PRELIMINARY;      PRT;   504 AA.
AC   O88885;
DT   01-NOV-1998 (TrEMBLrel. 08, Created)
DT   01-NOV-1998 (TrEMBLrel. 08, Last sequence update)
DT   01-MAR-2004 (TrEMBLrel. 26, Last annotation update)
DE   Sphingosine kinase (Fragment).
GN   Name=Sphk1; Synonyms=SPHK1a;
OS   Mus musculus (Mouse).
OC   Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;
OC   Mammalia; Eutheria; Rodentia; Sciurognathi; Muridae; Murinae; Mus.
OX   NCBI_TaxID=10090;
RN   [1]
RP   SEQUENCE FROM N.A.
RX   MEDLINE=98395082; PubMed=9726979; DOI=10.1074/jbc.273.37.23722;
RA   Kohama T., Olivera A., Edsall L., Nagiec M.M., Dickson R., Spiegel S.;
RT   "Molecular cloning and functional characterization of murine
RT   sphingosine kinase.";
RL   J. Biol. Chem. 273:23722-23728(1998).
DR   EMBL; AF068748; AAC61697.1; -.
DR   MGD; MGI:1316649; Sphk1.
DR   GO; GO:0004143; F:diacylglycerol kinase activity; IEA.
DR   GO; GO:0007205; P:protein kinase C activation; IEA.
DR   InterPro; IPR001206; DAGKc.
DR   Pfam; PF00781; DAGK_cat; 1.
DR   ProDom; PD005043; DAGKc; 1.
DR   SMART; SM00046; DAGKc; 1.
KW   Kinase.
FT   NON_TER       1       1
SQ   SEQUENCE   504 AA;  55119 MW;  2AAFEBA72027F509 CRC64;
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Best Local Similarity 81.2%; Pred. No. 1.3e-129;
Matches 306; Conservative 34; Mismatches 36; Indels 1; Gaps 1;

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Db       129 PRGLLPRPCRVLVLLNPQGGKGKALQLFQSRVQPFLEEAEITFKLILTERKNHARELVCA 188

Qy        67 EELGRWDALVVMSGDGLMHEVVNGLMERPDWETAIQKPLCSLPAGSGNALAASLNHYAGY 126

Db       189 EELGHWDALAVMSGDGLMHEVVNGLMERPDWETAIQKPLCSLPGGSGNALAASVNHYAGY 248

Qy       127 EQVTNEDLLTNCTLLLCRRLLSPMNLLSLHTASGLRLFSVLSLAWGFIADVDLESEKYRR 186

Db       249 EQVTNEDLLINCTLLLCRRRLSPMNLLSLHTASGLRLYSVLSLSWGFVADVDLESEKYRR 308

Qy       187 LGEMRFTLGTFLRLAALRTYRGRLAYLPVGRVGSKTPASPVVVQQGPVDAHLVPLEEPVP 246

Db       309 LGEIRFTVGTFFRLASLRIYQGQLAYLPVGTVASKRPAS-TLVQKGPVDTHLVPLEEPVP 367

Qy       247 SHWTVVPDEDFVLVLALLHSHLGSEMFAAPMGRCAAGVMHLFYVRAGVSRAMLLRLFLAM 306

Db       368 SHWTVVPEQDFLLVLVLLHTHLSSELFAAPMGRCEAGVMHLFYVRAGVSRAALLRLFLAM 427

Qy       307 EKGRHMEYECPYLVYVPVVAFRLEPKDGKGMFAVDGELMVSEAVQGQVHPNYFWMVSGCV 366

Db       428 QKGKHMELDCPYLVHVPVVAFRLEPRSQRGVFSVDGELMVCEAVQGQVHPNYLWMVCGSR 487
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Attachment, please send to applicant

; CURRENT FILING DATE: 1998-12-04
; EARLIER APPLICATION NUMBER: PCT/US98/11422
; EARLIER FILING DATE: 1998-06-04
; EARLIER APPLICATION NUMBER: 60/048,885
; EARLIER FILING DATE: 1997-06-06
; EARLIER APPLICATION NUMBER: 60/049,375
; EARLIER FILING DATE: 1997-06-06
; EARLIER APPLICATION NUMBER: 60/048,881
; EARLIER FILING DATE: 1997-06-06
; EARLIER APPLICATION NUMBER: 60/048,880
; EARLIER FILING DATE: 1997-06-06
; EARLIER APPLICATION NUMBER: 60/048,896
; EARLIER FILING DATE: 1997-06-06
; EARLIER APPLICATION NUMBER: 60/049,020
; EARLIER FILING DATE: 1997-06-06
; EARLIER APPLICATION NUMBER: 60/048,876
; EARLIER FILING DATE: 1997-06-06
; EARLIER APPLICATION NUMBER: 60/048,895
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; EARLIER APPLICATION NUMBER: 60/048,884
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; EARLIER APPLICATION NUMBER: 60/048,875
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; EARLIER APPLICATION NUMBER: 60/049,374
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; EARLIER APPLICATION NUMBER: 60/048,898
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; EARLIER APPLICATION NUMBER: 60/048,962
; EARLIER FILING DATE: 1997-06-06
; EARLIER APPLICATION NUMBER: 60/048,963
; EARLIER FILING DATE: 1997-06-06
; EARLIER APPLICATION NUMBER: 60/048,877
; EARLIER FILING DATE: 1997-06-06
; EARLIER APPLICATION NUMBER: 60/048,878
; EARLIER FILING DATE: 1997-06-06
; EARLIER APPLICATION NUMBER: 60/070,923
; EARLIER FILING DATE: 1997-12-18
; EARLIER APPLICATION NUMBER: 60/092,921
; EARLIER FILING DATE: 1998-07-15
; EARLIER APPLICATION NUMBER: 60/094,657
; EARLIER FILING DATE: 1998-07-30
; NUMBER OF SEQ ID NOS: 1227
; SOFTWARE: PatentIn Ver. 2.0
; SEQ ID NO 328
; LENGTH: 293
; TYPE: PRT
; ORGANISM: Homo sapiens
; FEATURE:
; NAME/KEY: SITE
; LOCATION: (36)
; OTHER INFORMATION: Xaa equals any of the naturally occurring L-amino acids
US-09-205-258-328

Query Match 76.3%; Score 1538; DB 4; Length 293;
Best Local Similarity 99.3%; Pred. No. 4.4e-165;
Matches 291; Conservative 1; Mismatches 1; Indels 0; Gaps 0;

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Qy         92 MERPDWETAIQKPLCSLPAGSGNALAASLNHYAGYEQVTNEDLLTNCTLLLCRRLLSPMN 151
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Qy        152 LLSLHTASGLRLFSVLSLAWGFIADVDLESEKYRRLGEMRFTLGTFLRLAALRTYRGRLA 211
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Db         61 LLSLHTASGLRLFSVLSLAWGFIADVDLESEKYRRLGEMRFTLGTFLRLAALRTYRGRLA 120

Qy        212 YLPVGRVGSKTPASPVVVQQGPVDAHLVPLEEPVPSHWTVVPDEDFVLVLALLHSHLGSE 271
               ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        121 YLPVGRVGSKTPASPVVVQQGPVDAHLVPLEEPVPSHWTVVPDEDFVLVLALLHSHLGSE 180

Qy        272 MFAAPMGRCAAGVMHLFYVRAGVSRAMLLRLFLAMEKGRHMEYECPYLVYVPVVAFRLEP 331
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Db        181 MFAAPMGRCAAGVMHLFYVRAGVSRAMLLRLFLAMEKGRHMEYECPYLVYVPVVAFRLEP 240

Qy        332 KDGKGMFAVDGELMVSEAVQGQVHPNYFWMVSGCVEPPPSWKPQQMPPPEEPL 384
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Db        241 KDGKGVFAVDGELMVSEAVQGQVHPNYFWMVSGCVEPPPSWKPQQMPPPEEPL 293
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RESULT 14
US-09-796-487-9
; Sequence 9, Application US/09796487
; Patent No. 6830916
; GENERAL INFORMATION:
; APPLICANT: Spiegel, Sarah
; TITLE OF INVENTION: Sphingosin Kinase, Cloning, Expression and Methods of Use
; FILE REFERENCE: 07320001aa (2033957-0001)
; CURRENT APPLICATION NUMBER: US/09/796,487
; CURRENT FILING DATE: 2001-03-02
; PRIOR APPLICATION NUMBER: US 60/186,532
; PRIOR FILING DATE: 2000-03-03
; PRIOR APPLICATION NUMBER: US 09/530,868
; PRIOR FILING DATE: 2000-05-05
; NUMBER OF SEQ ID NOS: 17
; SOFTWARE: PatentIn version 3.1
; SEQ ID NO 9
; LENGTH: 204
; TYPE: PRT
; ORGANISM: Unknown
; FEATURE:
; OTHER INFORMATION: Putative kinase sequence obtained by assembling sequences from
; OTHER INFORMATION: everal human ESTs (accession numbers D31133, AA232791, W63556, A
; OTHER INFORMATION: 081152 and AA026479).
; NAME/KEY: MISC_FEATURE
; LOCATION: (1)..(204)
; OTHER INFORMATION: Corresponding to peptide sequence Putative Human in Figure 2.
US-09-796-487-9